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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/561,877	08/02/2006	Michael G. Goggins	61506(71699)	1113

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EXAMINER	
WHISENANT, ETHAN C	

ART UNIT	PAPER NUMBER
1634	

MAIL DATE	DELIVERY MODE
06/22/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/561,877	GOGGINS ET AL.	
	Examiner	Art Unit	
	Ethan Whisenant	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-14 and 17-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 6-14 and 17-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 December 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

NON-FINAL ACTION

1. **A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed on 03 JUN 09 in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.** Claim(s) 1-4, 6-14 and 17-24 **is/are now pending.**,

Deleted: ¶

35 USC § 112 - 1ST PARAGRAPH

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

CLAIM REJECTIONS under 35 USC § 112- 1ST PARAGRAPH

3. Claim(s) 1-4, 6-14, 17 and 24 is/are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for diagnosing pancreatic cancer by detecting a methylated SPARC nucleic acid molecule which SPARC nucleic acid molecule comprises the nucleic acid sequence set forth in SEQ ID NO. 1, does not reasonably provide enablement for all cancers or all possible variants thereof.

In *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court considered the issue of enablement in molecular biology. The Court summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d)

the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims. The Court also stated that although the level of skill in molecular biology is high, results of experiments in molecular biology are unpredictable.

To begin, the scope of the claims encompasses diagnosing all cancers in all organisms and in all tissues. The specification provides working examples in which human pancreatic cancer cells are detected but fails to teach detecting cancer in other tissues (e.g. kidney, liver or lung). Neither does the specification teach detecting pancreatic caner or in other cancer in any animals (e.g. dogs, cats, horses, cows etc.) beyond humans. The prior art teaches numerous example of genes that are hypermethylated /hypomethylated and under expressed/ over expressed in certain cancers. See for example Polyak et al. [US 2002/0183501 (2002)] , Ueki et al. [Cancer Research 60 :1835-1839 (2000)] ; Matsubayashi et al. [Clinical Cancer Research 9 : 1466-1452 (APR 2003)] ; Sato et al. [Oncogene 22 : 5021-5030(2003)] ; Jansen et al. [Cancer Biology & Therapy 1 : 293-296 (2002)] ; Sato et al. [Gasterenterology 123 : 365-372 (2002)] ; Goelz et al. Science 228 : 187-190(1985) ; Baylin et al. Advances in Cancer Research 72 : 141-196 (1998) and Jones et al. [Nature Reviews Genetics 3 : 415-428 (JUN 2002)]. Finally, it is noted that specification teach SEQ ID NO: 1 but fails to teach any variants thereof. Accordingly, it is concluded that undue experimentation is required to make the invention as it is claimed. See M.P.E.P. §§ 706.03(n) and 706.03(z).

35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that may form the basis for rejections set forth in this Office action:

> A person shall be entitled to a patent unless --
> **(a)** the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> **(b)** the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> **(e)** the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
> or
> **(e)** the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

CLAIM REJECTIONS UNDER 35 USC § 102

5. **Claim(s) 1-3, 6-8, 13-14 and 17** is/are rejected under 35 U.S.C. 102(a) as being anticipated by Shuber [US 2003/0087258(2003)].

Claim 1 is drawn to a method of diagnosing cancer, comprising the detection of a methylated SPARC nucleic acid molecule or a variant thereof in a sample from a subject, wherein the methylated SPARC nucleic acid molecule comprises the nucleic acid sequence set forth in SEQ ID NO. 1.

Shuber teach a method of diagnosing cancer (i.e. colorectal cancer) in humans by detecting aberrent methylation in regulatory region of the H1C1 gene, p14 gene, the HLTF gene, the MINT2 gene, and/or the MINT31 gene, any of which could be termed of a variant of the SPARC gene comprising SEQ ID NO: 1.

Claim 2 is drawn to an embodiment of the method of Claim 1 wherein the presence of a methylated SPARC nucleic acid molecule is compared to a sample from a subject without cancer.

Shuber teach this limitation, see for example paragraph [0009].

Claim 3 is drawn to an embodiment of the method of Claim 1 wherein the sample is obtained from a mammal suspected to of having a proliferative cell growth disorder. presence of a methylated SPARC nucleic acid molecule is compared to a sample from a subject without cancer.

Shuber teach these limitation, see for example paragraph [0009] and [0014].

Claim 6 is drawn to an embodiment of the method of Claim 1 wherein a methylated SPARC nucleic acid molecule comprises a sequence having at least about 80% sequence identity to a molecule identified in SEQ ID NO:1. **Claim 7** is drawn to an embodiment of the method of Claim 1 wherein a methylated SPARC nucleic acid molecule comprises a sequence having at least about 90% sequence identity to a molecule identified in SEQ ID NO:1. **Claim 8** is drawn to an embodiment of the method of Claim 1 wherein a methylated SPARC nucleic acid molecule comprises a sequence having at least about 95% sequence identity to a molecule identified in SEQ ID NO:1.

Shuber teaches these limitation. Note where Shuber teach detecting aberrent methylation of CpG dinucleotides in the genes analyzed (i.e. a sequence having at least about 80% sequence identity to a molecule identified in SEQ ID NO:1, see the CpG dinucleotide at around residues 290-300). The CpG dinucleotides of Shuber thus have 100% identity to a molecule identified in SEQ ID NO:1.

Claim 13 is drawn to an embodiment of the method of Claim 1 wherein the subject sample is from a mammalian patient. **Claim 14** is drawn to an embodiment of the method of Claim 1 wherein the subject sample is from human patient. **Claim 17** is drawn to an embodiment of the method of Claim 1 wherein the methylated molecule is detected by methylation specific PCR.

Shuber teaches these limitations. See for example paragraph [0009], [0014] and [0032] – [0046].

35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligations under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claim Rejections under 35 USC § 103

8. **Claim(s) 4, 9-12 and 18-24** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Shuber [US 2003/0087258(2003)] as applied against Claims 1-3 and 6-8 above and further in view of Sato et al. [Oncogene 22 : 5021-5030 (2003)].

Claim 4 is drawn to an embodiment of the method of Claim 1 wherein the sample is obtained from a mammal suspected to of having a pancreatic cancer.

Shuber teach a method of diagnosing cancer in humans which comprises all of the limitations Claim 4 except these authors do not teach detecting pancreatic

cancer. However, Sato et al. do teach detecting aberrant methylation of the SPARC gene in pancreatic cancer cells. Therefore, absent an unexpected result it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method described by Shuber wherein the sample tested is a pancreatic tissue sample biopsy from a human patient suspected of having pancreatic cancer. The ordinary artisan would have been motivated to make the modification recited above in order to detect (i.e. diagnose) pancreatic cancer.

Claim 9 is drawn to an embodiment of the method of the method of Claim 1 wherein nucleic acid molecule is expressed at least a lower level in a patient with cancer as compared to expression levels in a normal individual. **Claim 10** is drawn to an embodiment of the method of Claim 1 wherein nucleic acid molecule is expressed at least about a 5-fold lower in a patient with cancer as compared to expression levels in a normal individual. **Claim 11** is drawn to an embodiment of the method of Claim 1 wherein nucleic acid molecule is expressed at least about a 10-fold lower in a patient with cancer as compared to expression levels in a normal individual.

Sato et al. teach these limitations, see the expression data shown in Figure 1 panel C.

Claim 12 is drawn to an embodiment of the method of Claim 1 wherein the cancer is a pancreatic cancer.

Sato et al. teach this limitation, see at least the abstract.

RESPONSE TO APPLICANT'S AMENDMENT/ ARGUMENTS

9. Applicant's arguments with respect to the claimed invention have been fully and carefully considered but are moot in view of the new ground(s) of rejection.

CONCLUSION

10. **Claim(s) 1-4, 6-14 and 17-24** is/are rejected and/or objected to for the reason(s) set forth above.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ethan Whisenant whose telephone number is (571) 272-0754. The examiner can normally be reached Monday-Friday from 8:30AM -5:30PM EST or any time via voice mail. If repeated attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz, can be reached at (571) 272-0763.

The Central Fax number for the USPTO is (571) 273-8300. Please note that the faxing of papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).

/Ethan Whisenant/
Primary Examiner
Art Unit 1634

EXAMINER SEARCH NOTES

16 JUN 09 - ECW

Databases searched: USPATFULL, USPG-PUBS, JAPIO and EUROPATFULL via EAST &

CAplus, Medline and BIOSIS via STN

Reviewed the parent(s), if any, and any search(es) performed therein : see the BIB data sheet

Reviewed, the search(es), if any, performed by prior examiners

Search terms:

STIC searched SEQ ID NO:1

Inventor(s) : e.g. Gogggins M?/au

Cancer$ or Carcinoma or adenocarcinoma or neoplasia
methylation
(gene or genes)
patient$
(control or controls)
diagnos$
PCR or methylation specific PCR
Bisulfite
Pancrea$